REMARKS

This application has been amended in a manner that is believed to place it in condition for allowance at the time of the next Official Action.

Claims 1-24 have been canceled. New claims 25-35 have been added. Support for new claims 25-35 may be found in previously pending claims 1-24.

The present invention is directed to isolated polyepitopes of the E6 protein of HPV, comprising 17 to 30 amino acids. The polyepitopes correspond to regions potentially able, when processed in the cytoplasm of presenting cells such as dendritic cells, to generate several epitopes that bind to various class I HLA molecules of types A and B.

As a result, these polyepitopes, or combinations thereof, are particularly interesting for their potential use for the treatment or the prevention of HPV infections and pathologies linked to these infections, as the polyepitopes confer protection to a very broad range of individuals of different class I HLA types.

In particular, claims 25-28 are all directed to a polyepitope from an E6 protein of human papillomavirus (HPV), comprising a peptide sequence wherein the number of amino acids is greater or equal to 17, and less or equal to 30, said peptide

sequence contains amino acid sequences of at least 5 different epitopes binding stably to HLA molecules of identical or different type, so that at least 6 HLA molecules of different types bind to these epitopes, said HLA molecules are selected from the group consisting of A1, A2, A3, A11, A24, A29, B7, B8, B18, B27, B35, B44 and B51, and wherein an epitope binding to HLA molecule of type B35, and an epitope binding to HLA molecule of type B44, and an epitope binding to HLA molecule of type B51 are present. Claims 29-35 are directed to polyepitopes having the elected sequence, SEQ ID NO: 6.

As a result, applicants believe that all of the claims are directed to a general inventive concept where there is a technical relationship among the inventions that involves at least one common or corresponding special technical feature. Indeed, as the Examiner is aware, the term special technical feature is defined as meaning those technical features that define the contribution which each claimed invention, considered as a whole, makes over the prior art.

As all of the claims are linked to a general inventive concept, applicants believe that all of the claims in their full scope should be examined.

The Examiner is also respectfully reminded that the United States Patent and Trademark Office published its policy for the examination of patent applications containing sequence

listings in the Official Gazette, 1192 O.G. 68 (November 19th, 1996). Applicants note that in establishing the new policy, the Commissioner has partially waived the requirements of 37 CFR 1.41 and will permit a reasonable number of sequences to be claimed and examined in a single application. Under this policy, up to 10 sequences may be examined in a single application without restriction. Indeed, Applicants believe that an examination of all the sequences found in claims 25-35 is in order.

As to the outstanding Official Action, the specification was objected to for not following the preferred layout for a patent application. The specification has been amended to incorporate the appropriate headings. As a result, it is believed that the specification is in good order.

Claims 1-4 and 6 were rejected under 35 USC §112, second paragraph, as allegedly being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. It is believed that the present amendment obviates this rejection.

In opposing the rejection, the outstanding Official Action alleged that these claims were indefinite for reciting the term "fragments". However, claims 25-35 have been drafted so that the term "fragments" is no longer recited in the claims. Moreover, the claimed polyepitopes relate to specific sequence

identification numbers. As a result, it is believed that claims 25-35 are definite to one of ordinary skill in the art.

Claim 6 was further rejected for reciting the term "corresponds". Claims 25-35 have also been drafted so that the term "corresponds" is no longer recited in the claims.

As a result, it is believed that claims 25-35 are definite to one of ordinary skill in the art.

Claims 1-4 were rejected under 35 USC §102(b) as allegedly being anticipated by MULLER et al. This rejection is respectfully traversed.

As the Examiner is aware, various immunolgical fates await any given antigen. If the antigen is present in circulating body fluids, such as blood or lymph, it can be taken up by B cells by means of its membranous antibodies, also called BCR (B cell receptor), or by antigen presenting cells (APCs), such as macrophages or dendritic cells. Once the antigen is taken up by these cells, it is processed in endosomes, that is, cut into small peptidic fragments, associated with class II HLA molecules and eventually presented at the surface of the cells under the form of a peptide-HLA complex.

Alternatively, if the antigen is found in cytoplasm, it can be processed therein and associated with class I HLA molecules to be presented at the surface of the cells.

Class II HLA molecules associated with an antigen fragment (T CD4 epitope) can activate T CD4 cells, which in turn can activate T CD8 cells, provided they are co-activated by class I HLA molecules associated with an antigen fragment (T CD8 epitope), or B cells, provided they are co-activated by a BCR antigen interaction (serological epitope).

Once activated, B cells produce antibodies and T cells carry their cytotoxic duties by destroying target cells which carry a corresponding CD8 epitope associated with a class I HLA molecule. For the Examiner's convenience a chart summarizing these immunological responses is enclosed with this amendment.

MULLER et al. disclose the use of HPV-16 E6 and E7 derived polypeptides as seroactive epitopes for the diagnosis of HPV-16 associated invasive cervical cancer, and the production of vaccines. The detection in human sera of antibodies directed to E6 and E7 is performed by ELISA. The epitopes described in this document are serological epitopes stimulating B cells for the production of antibodies giving rise to a serological response by formation of antigen-antibody complexes. These epitopes are not able to bind to class I HLA molecules and to stimulate T CD8 cells in the frame of a cellular response.

Among the various serological epitopes mentioned in this document, the serological epitopes (-5)-21 and 7-37 of the E6 protein are cited. MULLER et al. fail to disclose or suggest any

of the claimed sequences. Indeed, there is no mention of T CD8 epitopes in this document, nor any indication that T CD8 epitopes may be present in specific regions of the E6 protein.

Thus, applicants believe that MULLER et al. fail to disclose or suggest the claimed invention.

In the outstanding Official Action, claims 1-4 and 6 were rejected under 35 USC §102(b) as allegedly being anticipated by FRAZER et al. This rejection is respectfully traversed.

FRAZER et al. study T helper cell epitopes for generating an immune response against papillomavirus, the T helper cell epitopes correspond to epitopes 59-68 and 98-107 of the E6 protein. The publication does not disclose or suggest any of the claimed sequences.

The epitopes described in this document are T CD4 epitopes able to bind to class II HLA molecules and to stimulate T CD4 cells, which in turn can activate T CD8 cells, provided they are co-activated by class I HLA molecules associated with an antigen fragment (T CD8 epitope), or B cells, provided they are co-activated by a BCR antigen interaction (serological epitope), as mentioned above.

However, these T CD4 epitopes are not able to bind to class I HLA molecules and to stimulate T CD8 cells in the frame of a cellular response, as described in the present application.

Consequently, this document cannot anticipate or render obvious the claimed invention.

Claims 1-4 and 6 were then further rejected as allegedly being anticipated by MULLER et al. (Journal of General Virology, 71 (1990), 2709-2717).

This publication also fails to disclose or suggest any of the claimed sequences. As a result, it is believed that MULLER et al. fail to anticipate or render obvious the claimed invention.

Claims 1-4 were rejected under 35 USC §102(b) for allegedly being anticipated by MULLER et al. (EP 0523 391 A1). This rejection is respectfully traversed.

This document describes the fragments 1-23 and 8-37 of the E6 protein of HPV, and their use for the diagnosis of HPV infections.

The immune response involved in this document is of a serological type. The diagnosis of HPV infections is carried out by the detection of serological antibodies.

One again, there is no mention of the claimed sequences in this document.

Consequently, this document cannot anticipate the claimed invention. Furthermore, it cannot be obvious for one of ordinary skill in the art to modify the teachings of this document to obtain the claimed invention.

Claim 6 was rejected as allegedly being anticipated by VITIELLO et al. This rejection is respectfully traversed.

This document relates to compositions and methods for eliciting a cytotoxic T lymphocytes CTL immunity with peptides from HBV, HCV, HPV, HIV, MAGE-3, etc. According to this document, class I HLA epitopes must be used in combination with class II HLA epitopes. Epitopes 29-38 and 52-60 are described as individual T CD8 epitopes for illustration purpose.

There is no mention of the claimed polyepitopes. The publication does not disclose or suggest any of the claimed sequences.

Claims 1-4 and 6 were rejected under 35 USC §102(b) as allegedly being anticipated by DILLNER et al. This rejection is respectfully traversed. This document describes fragments of the E1 and E6 protein of HPV, and their use for the diagnosis of HPV infections.

As in the case of the EP 0 523 391 patent application mentioned above in the paragraph 4, the immune response involved in this document is of a serological type. The diagnosis of HPV infections is carried out by the detection of serological antibodies in an immunoassay.

One again, the publication does not disclose or suggest any of the claimed sequences.

As a result, applicants believe that DILLNER et al. fail to disclose or suggest the claimed invention.

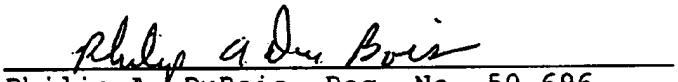
In view of the present amendment and the foregoing remarks, therefore, it is believed that this application is now in condition for allowance, with claims 25-35, as presented.

Allowance and passage to issue on that basis are accordingly respectfully requested.

The Commissioner is hereby authorized in this, concurrent, and future replies, to charge payment or credit any overpayment to Deposit Account No. 25-0120 for any additional fees required under 37 C.F.R. § 1.16 or under 37 C.F.R. § 1.17.

Respectfully submitted,

YOUNG & THOMPSON



Philip A. DuBois, Reg. No. 50,696
745 South 23rd Street
Arlington, VA 22202
Telephone (703) 521-2297
Telefax (703) 685-0573
(703) 979-4709

PD/mjr

APPENDIX:

The Appendix includes the following item:

- Chart of Immunological Responses